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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/521,691	08/31/2005	Masayasu Okochi	10873.1604USWO	4565

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EXAMINER	
BUNNER, BRIDGET E	

ART UNIT	PAPER NUMBER
1647	

MAIL DATE	DELIVERY MODE
01/07/2009	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/521,691	OKOCHI ET AL.	
	Examiner	Art Unit	
	Bridget E. Bunner	1647	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *1* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *20 October 2008*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-3 and 6-21* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☐ Claim(s) _____ is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☒ Claim(s) *1-3, 6-21* are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Status of Application, Amendments and/or Claims

The amendment of 20 October 2008 has been entered in full. Claims 1, 6, 7, 13, 15 are amended. Claims 19-21 are added.

Claims 1-3, 6-21 are pending in the instant application.

Election/Restrictions

After consideration of Applicant's amended and newly added claims submitted on 20 October 2008, the restriction requirement set forth between *claims* 1-5 and 6-11 only in the communication of 05 March 2008 is hereby withdrawn.

However, in view of the numerous SEQ ID NOs recited in the amended claims and in non-elected Groups II-XIX of the original restriction requirement of 05 March 2008, a subsequent restriction election is required.

REQUIREMENT FOR UNITY OF INVENTION

As provided in 37 CFR 1.475(a), a national stage application shall relate to one invention only or to a group of inventions so linked as to form a single general inventive concept ("requirement of unity of invention"). Where a group of inventions is claimed in a national stage application, the requirement of unity of invention shall be fulfilled only when there is a technical relationship among those inventions involving one or more of the same or corresponding special technical features. The expression "special technical features" shall mean those technical features that define a contribution which each of the claimed inventions, considered as a whole, makes over the prior art.

The determination whether a group of inventions is so linked as to form a single general inventive concept shall be made without regard to whether the inventions are claimed in separate claims or as alternatives within a single claim. See 37 CFR 1.475(e).

When Claims Are Directed to Multiple Categories of Inventions:

As provided in 37 CFR 1.475(b), a national stage application containing claims to different categories of invention will be considered to have unity of invention if the claims are drawn only to one of the following combinations of categories:

(1)A product and a process specially adapted for the manufacture of said product; or

(2)A product and process of use of said product; or

(3)A product, a process specially adapted for the manufacture of the said product, and a use of the said product; or

(4)A process and an apparatus or means specifically designed for carrying out the said process; or

(5)A product, a process specially adapted for the manufacture of the said product, and an apparatus or means specifically designed for carrying out the said process.

Otherwise, unity of invention might not be present. See 37 CFR 1.475(c).

1. Restriction is required under 35 U.S.C. 121 and 372.

This application contains the following inventions or groups of inventions which are not so linked as to form a single general inventive concept under PCT Rule 13.1.

In accordance with 37 CFR 1.499, applicant is required, in reply to this action, to elect a single invention to which the claims must be restricted.

Group 1. Claims 1-3, 6-11, 19-20, drawn to an isolated or synthesized Notch fragment polypeptide comprising an amino acid sequence of SEQ ID NO: 1.

Groups 2-18. Claims 1-3, 6-11, 19-20, drawn to an isolated or synthesized Notch fragment polypeptide comprising one amino acid sequence selected from the group consisting of SEQ ID NOs: 2-18. For example, if Group 3, is elected, the claims will be searched to the extent that they read upon SEQ ID NO: 3.

Groups 19-26. Claims 1-3, 21, drawn to an isolated or synthesized Notch fragment polypeptide comprising an amino acid sequence consisting of the 1st residue to the 8th residue of SEQ ID NOs: 37 or 38 or an amino acid sequence consisting of the 1st residue to the 6th residue of SEQ ID NOs: 39-44. For example, if Group 20 is elected, the claims will be searched to the extent that they read upon an amino acid sequence consisting of the 1st residue to the 8th residue of SEQ ID NO: 38.

The groups of inventions listed above do not relate to a single general inventive concept under PCT Rule 13.1 because, under PCT Rule 13.2, they lack the same or corresponding special technical features for the following reasons:

Groups 1-26 lack unity of invention because the groups do not share the same or corresponding technical feature. For example, the amino acid sequences of Groups 1-26 are composed of different amino acids and are structurally and functionally unrelated to each other. Accordingly, each of the 26 different amino acid sequences are not so linked under PCT Rule 13.1 and are thus placed in 26 different inventive Groups numbered 1-26, respectively. Additionally, SEQ ID NO: 1 is anticipated by prior art. Amino acid residues 1711-1731 of Genbank Accession No. Q01705 are 100% identical to amino acids 1-21 of SEQ ID NO: 1 of the instant application (see sequence alignment attached to the instant Office Action as Appendix A). Therefore, the amino acid sequence of SEQ ID NO: 1 lacks a special technical feature.

Applicant is advised that the reply to this requirement to be complete must include (i) an election of a species or invention to be examined even though the requirement may be traversed (37 CFR 1.143) and (ii) identification of the claims encompassing the elected invention.

The election of an invention or species may be made with or without traverse. To preserve a right to petition, the election must be made with traverse. If the reply does not distinctly and specifically point out supposed errors in the restriction requirement, the election shall be treated as an election without traverse. Traversal must be presented at the time of election in order to be considered timely. Failure to timely traverse the requirement will result in the loss of right to petition under 37 CFR 1.144. If claims are added after the election, applicant must indicate which of these claims are readable on the elected invention or species.

Should applicant traverse on the ground that the inventions have unity of invention (37 CFR 1.475(a)), applicant must provide reasons in support thereof. Applicant may submit evidence or identify such evidence now of record showing the inventions to be obvious variants or clearly admit on the record that this is the case. Where such evidence or admission is provided by applicant, if the examiner finds one of the inventions unpatentable over the prior art, the evidence or admission may be used in a rejection under 35 U.S.C. 103(a) of the other invention.

Applicant is reminded that upon the cancellation of claims to a non-elected invention, the inventorship must be amended in compliance with 37 CFR 1.48(b) if one or more of the currently named inventors is no longer an inventor of at least one claim remaining in the application. Any amendment of inventorship must be accompanied by a request under 37 CFR 1.48(b) and by the fee required under 37 CFR 1.17(i).

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Bridget E. Bunner whose telephone number is (571) 272-0881. The examiner can normally be reached on 8:30-4:30 M-F.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Manjunath Rao can be reached on (571) 272-0939. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

BEB
Art Unit 1647
02 January 2009

/Bridget E Bunner/
Primary Examiner, Art Unit 1647

Appendix A

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NOTC1_MOUSE
ID   NOTC1_MOUSE             Reviewed;        2531 AA.
AC   Q01705; Q06007; Q61905; Q99JC2; Q9QW58; Q9R0X7;
DT   01-NOV-1995, integrated into UniProtKB/Swiss-Prot.
DT   01-FEB-1996, sequence version 2.
DT   26-JUL-2007, entry version 92.
DE   Neurogenic locus notch homolog protein 1 precursor (Notch 1) (Motch A)
DE   (mT14) (p300) [Contains: Notch 1 extracellular truncation; Notch 1
DE   intracellular domain].
GN   Name=Notch1; Synonyms=Motch;
OS   Mus musculus (Mouse).
OC   Eukaryota; Metazoa; Chordata; Craniata; Vertebrata; Euteleostomi;
OC   Mammalia; Eutheria; Euarchontoglires; Glires; Rodentia; Sciurognathi;
OC   Muroidea; Muridae; Murinae; Mus.
OX   NCBI_TaxID=10090;
RN   [1]
RP   NUCLEOTIDE SEQUENCE [MRNA] (ISOFORM 1).
RC   TISSUE=Embryo;
RX   MEDLINE=93194170; PubMed=8449489; DOI=10.1006/geno.1993.1055;
RA   Franco del Amo F., Gendron-Maguire M., Swiatek P.J., Jenkins N.A.,
RA   Copeland N.G., Gridley T.;
RT   "Cloning, analysis, and chromosomal localization of Notch-1, a mouse
RT   homolog of Drosophila Notch.";
RL   Genomics 15:259-264(1993).
RN   [2]
RP   NUCLEOTIDE SEQUENCE [MRNA] OF 731-1899 (ISOFORM 2), AND DEVELOPMENTAL
RP   STAGE.
RC   STRAIN=CD-1; TISSUE=Embryo;
RX   MEDLINE=93050801; PubMed=1426644; DOI=10.1016/0012-1606(92)90076-S;
RA   Reaume A.G., Conlon R.A., Zirngibl R., Yamaguchi T.P., Rossant J.;
RT   "Expression analysis of a Notch homologue in the mouse embryo.";
RL   Dev. Biol. 154:377-387(1992).
RN   [3]
RP   NUCLEOTIDE SEQUENCE [MRNA] OF 1551-1647 (ISOFORM 1), AND DEVELOPMENTAL
RP   STAGE.
RC   TISSUE=Embryo;
RX   MEDLINE=93048835; PubMed=1425352;
RA   Franco del Amo F., Smith D.E., Swiatek P.J., Gendron-Maguire M.,
RA   Greenspan R.J., McMahon A.P., Gridley T.;
RT   "Expression pattern of Motch, a mouse homolog of Drosophila Notch,
RT   suggests an important role in early postimplantation mouse
RT   development.";
RL   Development 115:737-744(1992).
RN   [4]
RP   NUCLEOTIDE SEQUENCE [MRNA] OF 1161-1547.
RC   STRAIN=C57BL/6 X CBA; TISSUE=Embryo;
RX   MEDLINE=93178563; PubMed=8440332; DOI=10.1006/excr.1993.1044;
RA   Lardelli M., Lendahl U.;
RT   "Motch A and Motch B-two mouse Notch homologues coexpressed in a wide
RT   variety of tissues.";
RL   Exp. Cell Res. 204:364-372(1993).
RN   [5]
RP   NUCLEOTIDE SEQUENCE [MRNA] OF 1659-1673.
RX   MEDLINE=99364499; PubMed=10437788; DOI=10.1016/S0014-5793(99)00901-1;
RA   Lee J.S., Ishimoto A., Yanagawa S.;
RT   "Murine leukemia provirus-mediated activation of the Notch1 gene leads
RT   to induction of HES-1 in a mouse T lymphoma cell line, DL-3.";
RL   FEBS Lett. 455:276-280(1999).
RN   [6]
RP   NUCLEOTIDE SEQUENCE [MRNA] OF 1950-2201.
RX   MEDLINE=98029496; PubMed=9384671;
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RA Messerle M., Follo M., Nehls M., Eggert H., Boehm T.;
RT "Dynamic changes in gene expression during in vitro differentiation of
RT mouse embryonic stem cells.";
RL Cytokines Cell. Mol. Ther. 1:139-143(1995).
RN [7]
RP PROTEIN SEQUENCE OF 1655-1659, CLEAVAGE BY FURIN-LIKE CONVERTASE, AND
RP MUTAGENESIS OF 1651-ARG--ARG-1654.
RX MEDLINE=98318619; PubMed=9653148; DOI=10.1073/pnas.95.14.8108;
RA Logeat F., Bessia C., Brou C., LeBail O., Jarriault S., Seidah N.G.,
RA Israel A.;
RT "The Notch1 receptor is cleaved constitutively by a furin-like
RT convertase.";
RL Proc. Natl. Acad. Sci. U.S.A. 95:8108-8112(1998).
RN [8]
RP NUCLEOTIDE SEQUENCE [MRNA] OF 1865-2075, AND DEVELOPMENTAL STAGE IN
RP HAIR FOLLICLES.
RX PubMed=8486742; DOI=10.1083/jcb.121.3.631;
RA Kopan R., Weintraub H.;
RT "Mouse notch: expression in hair follicles correlates with cell fate
RT determination.";
RL J. Cell Biol. 121:631-641(1993).
RN [9]
RP PARTIAL PROTEIN SEQUENCE, AND PROTEOLYTIC PROCESSING.
RX MEDLINE=21523956; PubMed=11518718; DOI=10.1074/jbc.M107234200;
RA Saxena M.T., Schroeter E.H., Mumm J.S., Kopan R.;
RT "Murine notch homologs (N1-4) undergo presenilin-dependent
RT proteolysis.";
RL J. Biol. Chem. 276:40268-40273(2001).
RN [10]
RP PROTEOLYTIC PROCESSING.
RX MEDLINE=21374376; PubMed=11459941; DOI=10.1073/pnas.161269998;
RA Mizutani T., Taniguchi Y., Aoki T., Hashimoto N., Honjo T.;
RT "Conservation of the biochemical mechanisms of signal transduction
RT among mammalian Notch family members.";
RL Proc. Natl. Acad. Sci. U.S.A. 98:9026-9031(2001).
RN [11]
RP INTERACTION WITH DTX1 AND DTX2.
RX MEDLINE=21123790; PubMed=11226752; DOI=10.1016/S0736-5748(00)00071-X;
RA Kishi N., Tang Z., Maeda Y., Hirai A., Mo R., Ito M., Suzuki S.,
RA Nakao K., Kinoshita T., Kadesch T., Hui C.-C., Artavanis-Tsakonas S.,
RA Okano H., Matsuno K.;
RT "Murine homologs of deltex define a novel gene family involved in
RT vertebrate Notch signaling and neurogenesis.";
RL Int. J. Dev. Neurosci. 19:21-35(2001).
RN [12]
RP INTERACTION WITH MAML1.
RX PubMed=15019995; DOI=10.1016/j.gene.2003.12.007;
RA Wu L., Kobayashi K., Sun T., Gao P., Liu J., Nakamura M., Weisberg E.,
RA Mukhopadhyay N.K., Griffin J.D.;
RT "Cloning and functional characterization of the murine mastermind-like
RT 1 (Maml1) gene.";
RL Gene 328:153-165(2004).
RN [13]
RP INTERACTION WITH DNER, FUNCTION, AND TISSUE SPECIFICITY.
RX PubMed=15965470; DOI=10.1038/nn1492;
RA Eiraku M., Tohgo A., Ono K., Kaneko M., Fujishima K., Hirano T.,
RA Kengaku M.;
RT "DNER acts as a neuron-specific Notch ligand during Bergmann glial
RT development.";
RL Nat. Neurosci. 8:873-880(2005).
RN [14]
RP X-RAY CRYSTALLOGRAPHY (2.2 ANGSTROMS) OF 1970-2104.
RX PubMed=15802643; DOI=10.1110/ps.041184105;
RA Lubman O.Y., Kopan R., Waksman G., Korolev S.;
RT "The crystal structure of a partial mouse Notch-1 ankyrin domain:
RT repeats 4 through 7 preserve an ankyrin fold.";
RL Protein Sci. 14:1274-1281(2005).

```
CC   -!- FUNCTION: Functions as a receptor for membrane-bound ligands
CC       Jagged1, Jagged2 and Delta1 to regulate cell-fate determination.
CC       Upon ligand activation through the released notch intracellular
CC       domain (NICD) it forms a transcriptional activator complex with
CC       RBP-J kappa and activates genes of the enhancer of split locus.
CC       Affects the implementation of differentiation, proliferation and
CC       apoptotic programs (By similarity). May play an essential role in
CC       postimplantation development, probably in some aspect of cell
CC       specification and/or differentiation. May be involved in mesoderm
CC       development, somite formation and neurogenesis. Involved in the
CC       maturation of both CD4+ and CD8+ cells in the thymus. Important
CC       for follicular differentiation and possibly cell fate selection
CC       within the follicle. During cerebellar development, functions as a
CC       receptor for neuronal DNER and is involved in the differentiation
CC       of Bergmann glia.
CC   -!- SUBUNIT: Heterodimer of a C-terminal fragment N(TM) and an N-
CC       terminal fragment N(EC) which are probably linked by disulfide
CC       bonds. Interacts with DNER, DTX1, DTX2 and RBPSUH. Also interacts
CC       with MAML1, MAML2 and MAML3 which act as transcriptional
CC       coactivators for NOTCH1.
CC   -!- SUBCELLULAR LOCATION: Cell membrane; Single-pass type I membrane
CC       protein. NICD: Nucleus. Note=Following proteolytical processing
CC       NICD is translocated to the nucleus.
CC   -!- ALTERNATIVE PRODUCTS:
CC       Event=Alternative splicing; Named isoforms=2;
CC       Name=1;
CC         IsoId=Q01705-1; Sequence=Displayed;
CC       Name=2;
CC         IsoId=Q01705-2; Sequence=VSP_001402, VSP_001403, VSP_001404;
CC         Note=No experimental confirmation available;
CC   -!- TISSUE SPECIFICITY: Highly expressed in the brain, lung and
CC       thymus. Expressed at lower levels in the spleen, bone-marrow,
CC       spinal cord, eyes, mammary gland, liver, intestine, skeletal
CC       muscle, kidney and heart. In the hair follicle, highly expressed
CC       exclusively in the epithelial compartment.
CC   -!- DEVELOPMENTAL STAGE: First detected in the mesoderm at 7.5 dpc By
CC       8.5 dpc highly expressed in presomitic mesoderm, mesenchyme and
CC       endothelial cells, while much lower levels are seen in the
CC       neuroepithelium. Between 9.5-10.5 dpc expressed at high levels in
CC       the neuroepithelium. At 13.5 dpc expressed in the surface
CC       ectoderm, eye and developing whisker follicles. Hair follicle
CC       matrix cells expression starts as different cell types become
CC       distinguishable in the developing follicle. Expression persists
CC       throughout the growth phase of the follicle and maintains the same
CC       expression profile in the second hair cycle. The cells in the
CC       follicle that undergo a phase of high level expression are in
CC       transition from mitotic precursors to several discrete,
CC       differentiating cell types. Specifically expressed in cerebellar
CC       Bergmann glial cells during post-natal development.
CC   -!- PTM: Synthesized in the endoplasmic reticulum as an inactive form
CC       which is proteolytically cleaved by a furin-like convertase in the
CC       trans-Golgi network before it reaches the plasma membrane to yield
CC       an active, ligand-accessible form. Cleavage results in a C-
CC       terminal fragment N(TM) and a N-terminal fragment N(EC). Following
CC       ligand binding, it is cleaved by TNF-alpha converting enzyme
CC       (TACE) to yield a membrane-associated intermediate fragment called
CC       notch extracellular truncation (NEXT). This fragment is then
CC       cleaved by presenilin dependent gamma-secretase to release a
CC       notch-derived peptide containing the intracellular domain (NICD)
CC       from the membrane.
CC   -!- PTM: Phosphorylated.
CC   -!- SIMILARITY: Belongs to the NOTCH family.
CC   -!- SIMILARITY: Contains 5 ANK repeats.
CC   -!- SIMILARITY: Contains 36 EGF-like domains.
CC   -!- SIMILARITY: Contains 3 LNR (Lin/Notch) repeats.
CC   ---------------------------------------------------------------------
CC   Copyrighted by the UniProt Consortium, see http://www.uniprot.org/terms
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CC   Distributed under the Creative Commons Attribution-NoDerivs License
CC   -----------------------------------------------------------------------
DR   EMBL; Z11886; CAA77941.1; -; mRNA.
DR   EMBL; L02615; AAK14898.1; -; mRNA.
DR   EMBL; X68278; CAA48339.1; -; mRNA.
DR   EMBL; AJ238029; CAB40733.1; -; mRNA.

  Query Match           100.0%;  Score 108;  DB 1;  Length 2531;
  Best Local Similarity  100.0%;  Pred. No. 9.6e-07;
  Matches   21;  Conservative    0;  Mismatches    0;  Indels    0;  Gaps    0;

Qy          1 VKSEPVEPPLPSQLHLMYVAA 21
              |||||||||||||||||||||
Db       1711 VKSEPVEPPLPSQLHLMYVAA 1731
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